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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,410	07/26/2001	Ulrich Martin	05882.0002.CNUS01	1409

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/917,410	MARTIN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,23,27 and 29-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,23,27 and 29-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of the species (A), wherein the L-selectin antibody comprises SEQ ID NO: 2 and 4 with traverse in the Response to Restriction Requirement, filed 11/3/03, is acknowledged.

In the interest of compact prosecution, the previous species election has been withdrawn.

Claims 1-19 are pending and being acted upon presently.

2. In response to the previous Office Action, applicant has provided the following clarification in Response to Restriction Requirement, filed 11/3/03.

The recitation "mulitple organ failure of a patient after a polytraumatic event" is the failure of more than one organ following an event that results in a simultaneously acquired injury of at least two or more organ systems. Injuries resulting from a polytraumatic event are immediately life threatening due to the combination of the injured organ systems or due to the fact that one of the at least two injuries is per se life threatening. The recitation "multiple organ failure of a patient after a severe polytraumatic event" is the failure of more than one organ following an extremely intense event that results in a simultaneously acquired injury of at least two or more organ systems. For example, the recitation of "multiple organ failure of a patient after a polytraumatic event" does not read on ischemia-reperfusion if the ischemia-reperfusion did not result from a "a polytraumatic event".

It is acknowledged that the preamble of claims 1, 8 and 14 give life and meaning to the manipulative steps of the claims. Therefore, the preamble of claims 1, 8 and 14 defines the patient as one who has suffered a polytraumatic event or a severe polytraumatic event.

3. The filing date of the recitation of "from 0.5 hours to **4** hours" in claims 2 and 9 appears to be the filing date of PCT/US96/13152, filed 8/13/96, as the previous priority documents provide written description for "from 0.5 hours to **3** hours" and not "from 0.5 hours to **4** hours".

The filing date of the recitation of SEQ ID NOS. in claims 6, 7, 12, 13, 18 and 19 appears to be the filing date of PCT/US96/13152, filed 8/13/96, as the previous priority documents do not provide written description for SEQ ID NOS: 2, 4, 5 and 6.

If applicant desires priority prior to 8/13/96 for these "limitations"; applicant is invited to point out and provide documentary support for the priority of the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

The priority date of claims 1, 3-5, 8, 10, 11, 14-17 appears to be the filing date of USSN 08/578,953, filed 12/27/95.

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in USSN 08/578,953. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Applicant is required to identify the nucleotide and amino acid sequences in the specification with SEQ. ID NOS.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required.

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 5, 11 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that the HuDreg 55 or HuDreg 200 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines / hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Alternatively, it is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific HuDreg 44 and HuDreg 200 antibodies requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences.

Therefore, applicant is invited to consider amending the claims to recite the appropriate SEQ ID NOS. that identify the specific HuDreg 44 and HuDreg 200 antibodies.

7. Claims 1-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-19 are indefinite in the recitation of "prevention of multiorgan failure after a polytraumatic event" and "treating a patient who has suffered a severe polytraumatic event" because the metes and bounds of said "polytraumatic event" are ill-defined and ambiguous.
Further, the distinction between a "polytraumatic event" and a "severe polytraumatic event" is not clearly defined.

In addition, the therapeutic endpoints of "prevention of multiorgan failure after a polytraumatic event" and "treating a patient who has suffered a severe polytraumatic event" are ill-defined and ambiguous.

As indicated above, in response to the previous Office Action, applicant has provided the following clarification in Response to Restriction Requirement, filed 11/3/03, as reiterated herein.

The recitation "mulitple organ failure of a patient after a polytraumatic event" is the failure of more than one organ following an event that results in a simultaneously acquired injury of at least two or more organ systems. Injuries resulting from a polytraumatic event are immediately life threatening due to the combination of the injured organ systems or due to the fact that one of the at least two injuries is per se life threatening. The recitation "multiple organ failure of a patient after a severe polytraumatic event" is the failure of more than one organ following an extremely intense event that results in a simultaneously acquired injury of at least two or more organ systems. For example, the recitation of "multiple organ failure of a patient after a polytraumatic event" does not read on ischemia-reperfusion if the ischemia-reperfusion did not result from a "a polytraumatic event".

However, applicant has not provided sufficient nexus to the specification as filed, nor has applicant has provided objective evidence to support applicant's clarification of the metes and bounds of the claimed methods.

In addition, applicant's clarification indicates that the recitation "multiple organ failure of a patient after a severe polytraumatic event" is the failure of more than one organ following an extremely intense event that results in a simultaneously acquired injury of at least two or more organ systems. However, the phrase "extremely intense event" is relative in nature, which renders the distinction between a "polytraumatic event" and a "severe polytraumatic event" indefinite. The phrase "extremely intense event" is not defined by the claims; the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Also, applicant is invited to clarify the metes and bounds of "prevention of multiorgan failure after a polytraumatic event" and "treating a patient who has suffered a severe polytraumatic event", including the targeted patient populations, the therapeutic endpoints and the difference(s) between a "traumatic event" and a "severe traumatic event".

For example, are the claims limited to the prevention of multiple organ failure and to the considerable reduction of the mortality rate of polytrauma patients, as disclosed on page 5, paragraph 3 and page 9, paragraph 2 of the instant specification ?

For example, are the claimed methods met by treating hemorrhagic shock or multiorgan failure?

B) Claims 7, 8, 21, 27 are indefinite in the recitation of "Dreg 55 or HuDreg 55, HuDreg 200" because their characteristics are not known. The use of "these terms" as the sole means of identifying the claimed antibodies renders the claim indefinite because "these terms" are merely laboratory designations which do not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas. Applicant should amend the claims to include the SEQ ID NOS. to clearly identify the biological species.

C) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-19 are rejected under 35 U.S.C. § 103 as being unpatentable over Co (WO 94/12215) (1449) in view of Walt et al. (World Journal of Surgery 7: 164-166, 1983).

The instant claims are drawn to using L-selectin-specific antibodies in the treatment of patients who have suffered polytrauma.

Co teaches the therapeutic and prophylactic use of humanized DREG 55 and DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. cerebral ischemic event, brain surgery, shock, sepsis, adult respiratory distress syndrome, multiple organ failure as well as injuries dues to trauma; see page 29, paragraph 1) and dosages which depend on the patient and therapeutic endpoint, including doses of 0.01 - 10 mg and 0.3 - 3 mg/kg, including repeated doses (see entire document, particularly Methods of Use on pages 29-36).

Co et al. differs from the claimed invention by not disclosing the disorders or conditions such as shock, sepsis and multiple organ failure are resultant of polytrauma.

Walt et al. teach the hemorrhagic shock, cardiopulmonary failure and sepsis are the patients' greatest enemies in the treatment of multiple trauma patients (see entire document, including page 165, column 2, paragraph 2).

Co differs from the instant claimed methods by not disclosing all of the time points for administering the inhibitory L-selectin antibodies recited in the claims. However, as indicated herein, Co does teach dosages encompassed by the claimed methods. Further, it would have been standard practice by the ordinary artisan at the time the invention was made to provide dosages and modes of administration upon the needs of the patient and the nature of the intended therapeutic endpoint. Co does teach single and multiple administrations sufficient to cure or at least partially arrest the disease and its complications; which would depend on the severity of the disease and general state of the of the immune system in a patient; which can be administered as bolus or repeated injections to achieve optimal plasma levels of antibody and alone or in combination with other therapeutic agents or drugs (see Methods of Use).

Therefore, the prior art made and used L-selectin antibodies including the DREG 55 and DREG 200 specificities to inhibit inflammation including those associated with neutrophil adhesion and activation and the nature of the injuries claimed in the instant methods. The particular humanized L-selectin antibodies were known in the prior art or could have been made by routine technology at the time the invention was made. Although some of the references are silent about the exact sequences of the L-selectin-specific antibodies, the standard recombinant techniques and computer analyses of CDR known in the prior art would have resulted in the same or very nearly the same structural and functional characteristics of the instant claims since both the references and instant invention use the same techniques, the same antibody specificities and the same goals. For example, see the humanization of antibodies taught by Co and Lefer. Also, such humanization of antibodies for therapeutic uses was well known and practiced at the time the invention was made. The claimed functional limitations encompassed by the claims would be expected properties of selecting for L-selectin-specific antibodies to specifically bind and inhibit L-selectin.

The claims drawn to specifically defined humanized antibodies are obvious since the record does not contain any evidence that the antibodies differ in any significant manner that one of ordinary skill in the art would expect to generate using L-selectin as the starting antigen in the basic method of generating antibodies and humanizing said antibodies.

There appears no evidence that the use of various sources of framework amino acids would differ in an unexpected or distinct manner from those available to the ordinary artisan at the time the invention was made. Also, Co teaches the same DREG 55/DREG 200 antibodies of the claimed invention.

Given the teachings of Co directed to the therapeutic and prophylactic use of humanized DREG 55 and DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. cerebral ischemic event, brain surgery, shock, sepsis, adult respiratory distress syndrome, multiple organ failure as well as injuries dues to trauma; see page 29, paragraph 1 and page 30, paragraph 2), one of ordinary skill in the art would have targeted the same conditions in patients undergoing polytrauma, as shock, cardiopulmonary failure and sepsis are the patients' greatest enemies in the treatment of multiple trauma patients, as taught by Walt et al. (see entire document, including page 165, column 2, paragraph 2). Note, too, that Co et al. does teach treating patients with injuries due to trauma (see page 29, paragraph 1).

One of ordinary skill in the art at the time the invention was made would have been motivated to treat patients undergoing various cardiovascular procedures wherein extracorporeal circulation through a heart-lung machine is routinely employed by providing anti-L-selectin antibodies to inhibit neutrophil-mediated inflammatory responses in patients undergoing such cardiovascular procedures. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22, 23, 27, 29-40 of copending application USSN 09/013,871. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of both applications are drawn to the same or essentially the same methods of targeting patients after a polytraumatic event.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PHILLIP GAMBEL

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